

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Sven Schreder et al.

Group Art Unit: 1631

Serial No.: 09/700,421

Examiner: Phyllis G Spivack

Filed: November 15, 2000

For: Pharmaceutical Preparation

**DECLARATION UNDER 37 C.F.R. § 1.132**

Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

SIR:

Achim Schäffler, being duly warned, deposes and says:

I am a citizen of Germany;

I am a pharmacist by training and experience;

from 1988 to 1990 I was postgraduate at the Boehringer Ingelheim KG, Ingelheim, Germany;

the degree of D. Phil. was bestowed on me by the University Heidelberg, Germany in 1990;

from January 1991 to April 1991 I was employee at Schwarz Pharma AG, Monheim, Germany;

since May 1991 I have been with Merck KGaA, Darmstadt;

since September 1997 I've been in charge of the Pharmaceutical Development Department of Merck KGaA, Darmstadt, Germany; and since August 2002 I've got responsibility on Global Pharm Development of Merck KGaA.

The test results presented below for the present application prove that the claimed pharmaceutical preparation has an improved storage stability compared to the preparations known in the art.

I have carried out, or supervised experiments for preparation and stability testing of pharmaceutical preparations according to the methods described within the genus claimed in the pending application.

### **Experimental Report**

#### **Compositions and Preparation of Formulations used for Stability Testing**

| Ingredients           | Formulation A | Formulation B |
|-----------------------|---------------|---------------|
| Levothyroxine Sodium  | 0.105 mg      | 0.100 mg      |
| Lactose monohydrate   | 65.90 mg      | 67.40 mg      |
| Maize starch          | 25.00 mg      | 25.00 mg      |
| Gelatin               | 5.00 mg       |               |
| HPMC                  |               | 3.50 mg       |
| Croscarmellose Sodium | 3.50 mg       | 3.50 mg       |
| Magnesium Stearate    | 0.50 mg       | 0.50 mg       |

The compositions of formulations A and B were processed to tablets as described in Example 1 of the present application. Please note that composition of formulation A is identical to composition of Example 2 of the present application. The amount of HPMC (hydroxypropylmethylcellulose) in formulation B was adapted to achieve the same binding effect as achieved by gelatin.

Stability testing

The content of each formulations were measured before and after storage at 25°C / 60 % r.H. and 30°C / 75 % r.H., respectively using a reversed phase HPLC method and UV detection. The results obtained are presented in the following table:

| Storage time and conditions  | Levothyroxine Sodium Content |               |
|------------------------------|------------------------------|---------------|
|                              | Formulation A                | Formulation B |
| 0 (before storage)           | 105.1 µg                     | 99.4 µg       |
| 26 weeks at 25°C / 60 % r.H. | 100.2 µg                     | 89.3 µg       |
| 26 weeks at 30°C / 75 % r.H. | 99.3 µg                      | 72.3 µg       |

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

14.02. 2002  
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Date

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Achim Schäffler